Attorney Docket No. 119929-1031

Application No.: 09/846,727 Amendment dated February 2, 200

Reply to Office Action mailed November 2, 2005

Listing of Claims

This listing of claims will replace all prior versions, and listing, of claims in the Application.

(Currently Amended) A method for preparing a tracer composition comprising:
obtaining a ¹³C labeled Krebs cycle metabolite precursor that will produce an analyte;
and

obtaining a deuterium source,

wherein <u>gluconeogenesis</u> gluconeogenensis is measured from a subject that was provided the precursor and the deuterium source, and produced the analyte, by comparison of the relative nuclear magnetic resonance <u>signal areas</u> profiles in a spectrum obtained from of the labeled components in the analyte.

- 2. (Original) The method of claim 1, wherein the analyte is ¹³C-glucose.
- 3. (Currently Amended) The method of claim 1, wherein the <u>precursor</u> is glucose, lactase or alanine.
- 4. (Original) The method of claim 1, wherein the deuterium source is deuterated water.
- 5. (Currently Amended) The method of claim 1, wherein the analyte is glucose deuterated in the 2, 5 and 6<u>S</u> positions, and any transformation <u>in glucose</u> that maintains the 2,5 and 6 positions in relation to one another.
 - 6. (Original) The method of claim 1, wherein the analyte is $(1-6^{13}C_2)$ -glucose.
- 7. (Currently Amended) The method of claim $\underline{4}$ 1, wherein the <u>deuterated</u> water is D_2O .
- 8. (Previously Presented) The method of claim 1, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.
- 9. (Original) The method of claim 1, wherein the analyte is ¹³C-labeled glucose with the label at the 2 or 5 positions, or at both positions.
- 10. (Original) The method of claim 9, wherein the metabolite is a transformation of the labeled glucose containing the labeled 2 position, or the labeled 5 position, or both.

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- 11. (Currently Amended) The method of claim 1, further comprising the step of adding [¹³C₃]propionate ¹³C₃-propionate.
- 12. (Currently Amended) The method of claim 1, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, and beta-hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.
- 13. (Original) The method of claim 1, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.
 - 14. 15. (Canceled)
 - (Currently Amended) A method for preparing a tracer composition comprising: obtaining a deuterium source,

wherein <u>gluconeogenesis</u> gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance <u>signal areas</u> profiles in a spectrum obtained from of the deuterium components in the analyte, wherein the analyte is selected from the group consisting of glucose deuterated in the 2, 5 and 6 positions and deuterated glucose with any transformation that maintains the 2,5 and 6 positions in relation to one another.

(Currently Amended) A method for preparing a tracer composition comprising: obtaining a deuterium source,

wherein gluconeogenesis gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance signal areas profiles in a spectrum obtained from of the deuterium components in the analyte, wherein the analyte is (1-6 ¹³C₂)-glucose.

(Previously Presented) The method of claim 16, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.

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(Currently Amended) A method for preparing a tracer composition comprising:

obtaining a deuterium source;

wherein gluconeogenesis gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance signal areas profiles in a spectrum obtained from of the deuterium components in the analyte, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

(Currently Amended) A method for preparing an isotopic metabolic flux tracer composition comprising:

providing a ¹³C labeled Krebs cycle metabolite precursor to a subject to produce an analyte;

obtaining a sample from the subject; and

measuring the nuclear magnetic resonance signals of the labeled tracers sample to determine the rate of gluconeogenesis.

(Original) The method of claim 20, wherein the analyte is ¹³C-glucose.

20 22. (Original) The method of claim 20, wherein the analyte is glucose labeled with ¹³C at positions 1 through 6, or combinations of two or more at any position.

21 23. (Original) The method of claim 26, wherein the analyte is $(1-6^{13}C_2)$ -glucose.

22-24. (Original) The method of claim 28, wherein the sample is from blood, urine or tissue extracts.

23 25. (Currently Amended) The method of claim 20, further comprising the step of providing the subject with [13C₃]propionate ¹³C₃-propionate.

24 26. (Currently Amended) The method of claim 20, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, beta-hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.

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(Original) The method of claim 20, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

16 28. (Original) The method of claim 20, wherein the ¹³C Krebs cycle precursor is provided orally.

29. - 58. (Canceled).

(Currently Amended) A method for preparing a tracer composition comprising:

obtaining a deuterium source;

wherein <u>gluconeogenesis</u> <u>gluconeogenensis</u> is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance <u>signal areas</u> <u>profiles</u> <u>in a spectrum obtained from of the deuterium components in the analyte, and</u>

wherein the analyte is glucose deuterated in the 2, 5 and 6 positions, and any transformation of glucose that maintains the 2,5 and 6 positions in relation to one another, and

wherein the analyte is produced in the blood, urine or tissue.

16 60. (Previously Presented) The method of claim 1, wherein the analyte is produced in the blood, urine or tissue.

19 67. (Currently Amended) A method for preparing an isotopic metabolic flux tracer composition comprising:

providing a ¹³C labeled Krebs cycle metabolite precursor to a subject to produce an analyte;

obtaining a sample from the subject; and

measuring the nuclear magnetic resonance of the labeled tracers in the sample to determine the rate of gluconeogenesis,

wherein the analyte is ¹³C-glucose.

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M. (Previously Presented) The method of claim 17, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.

3 \ 63. (Previously Presented) The method of claim 19, wherein nuclear magnetic resonance profiles are used to measure flux selected from the group consisting of pyruvate recycling, anaplerotic, gluconeogenic, and combinations thereof.